PATENT
2786-0168P

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant:	Zurit LEVINE et al.	Conf.:	9282
Appl. No.:	09/805,020	Group:	1642
Filed:	March 13, 2001	Examiner:	Sheela Huff
For:	SPLICE VARIANTS OF ONCOGENES		

DECLARATION UNDER 37 CFR 1.132

Commissioner for Patents
P.O. Box 1450
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Sir:

I, Dr. Jeanne Bernstein, am an inventor in the present application.

I am familiar with the application and the various rejections in the Office Action mailed April 14, 2004. I would like to respond to the Examiner's rejections in view of her request for a Declaration stating Applicants' arguments.

Claims 3, 4, 13(in-part), 15 and 17 have been rejected by the Examiner under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility or a well-established utility. Claims 3, 4, 13(in-part), 15 and 17 have been rejected by the Examiner under 35 U.S.C. 112, first paragraph, because one skilled in the art would not know how to use the claimed invention because the claimed invention is not

supported by either a substantial asserted utility or a well-established utility.

The present invention as recited in claim 3 relates to an amino acid sequence selected from the group consisting of:

(i) an amino acid sequence coded by the isolated nucleic acid sequence of SEQ ID NO:36: and

(ii) and amino acid sequence according to SEQ ID NO:72.

Accordingly, the invention has been limited to an amino acid sequence coded by the isolated nucleic acid sequence of SEQ ID NO:36 or to an amino acid sequence according to SEQ ID NO:72.

The Examiner should note that the nucleic acid sequence of SEQ ID NO:36 corresponds to NV-36. Further, the Table starting on page 23 of the specification clearly identifies the function of the variant NV-36 under examination, that is, the amino acid sequence of SEQ ID NO 72 or nucleic acid sequence of SEQ ID NO 36. In the Table, the variants are listed in the same order as the sequences provided in the sequence listing. Therefore, it is clear that NV-36 corresponds to SEQ ID NO 36.

Further, the Table clearly shows that NV-36 is a variant of KPCT_HUMAN, and that *"the new variant has an alternative 3' exon of 36 amino acids instead of 94 original amino acids. The alternative region is in the PROTEIN KINASE domain. The new variant maintains the two PHORBOL-ESTER AND DAG BINDING domains, the two ATP binding sites and the ACTIVE of the KINASE domain"*.

KPCT_HUMAN is a known protein; for example, entering this information to the SwissProt database (for which KPCT_HUMAN identifies the record of this protein) results in a complete description of this protein being provided.

The known protein is Protein Kinase C (PKC), theta type, which phosphorylates a wide variety of proteins when activated. PKC is also involved as an oncogene; for example, it can be activated by a group of chemicals called phorbol esters, which are known tumor promoters. This information is also provided further in the text of the present application.

Both textual and graphical descriptions of the domains of PKC are provided in this record. These descriptions enable one of ordinary skill in the art to easily understand the description of the NV-36 variant according to the present invention.

Since the variant has a different protein kinase domain, but otherwise maintains the other domains of PKC, it is expected that protein kinase activity is affected but not abolished, since the active site *of* the protein kinase domain is still present.

Figure 36 shows the alignment of the known PKC sequence and of the sequence *of* the NV-36 variant according to the present invention, showing the differences between the sequences.

The utility of the NV-36 variant is therefore clearly

linked to the similarity/differences between this protein and the known PKC (theta) protein. As noted above, the variant protein differs in the kinase domain (while still having the active site), and therefore could be used to study the structure of this domain and its function, for example. Such information would clearly be useful for developing new drugs that could modulate PKC activity and/or activity of other kinases. Such utility is proposed in the present application.

Furthermore, the NV-36 variant could also be useful for studying the location and function of these proteins as oncogenes vs. their desired physiological activities; for example, PKC (theta) is highly expressed in hematopoietic cells, such that the NV-36 variant could be useful for studying both blood cancers and also the genesis of blood cells. The former activity is clearly non-desirable, while the latter activity is desirable, such that the NV-36 variant could be useful to understand and interpret the differences between these activities. PKC (theta) is present in platelets, which also have both desirable and potentially pathological activities, depending upon other factors in the body; NV-36 could also be useful for an understanding of the differences between these different activities.

The Bork reference mentioned by the Examiner on page 4 of the Action is not contradictory to the above statements. Bork

refers to overall statistical probability for sequence comparison. However, the degree of reliability of sequence/function data for different proteins clearly depends upon the degree to which they have been studied. Proteins that have been well studied and characterized, particularly those belonging to well-characterized protein families, clearly have more reliable associated functional and structural data. Protein kinases, especially those belonging to the protein kinase C family, are exceptionally well studied and characterized proteins. For example, protein kinases have their own publicly available database, called Kinbase (available at http://198.202.68.14/), which shows that a large amount of information has been collected about such kinases throughout a wide variety of organisms. These kinases have been subjected to extensive analyses. The PKC family itself is of great interest to researchers, because of its known involvement in a wide variety of intracellular signalling pathways and also because of its involvement in various cancers. For example a search of PubMed with the term "PKC" turned up 17997 references. Thus, the Bork reference is not relevant to the particular case of PKC and the NV-36 variant of the present invention, because of the extensive studies that have been performed on the PKC family.

Similarly, general statements of uncertainty regarding protein chemistry are not applicable to the PKC family for the

above reasons.

Thus, the NV-36 variant of the present invention clearly has utility, which is well expressed in the present application. Furthermore, as the above statements clarify, the present application also provides a clear description of how to use the NV-36 variant according to the present invention, thereby overcoming the rejections under 35 U.S.C 101/112.

I hereby declare that all statements made herein of my own knowledge are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 5/10/2004

BY _____
Dr. Jeanne Bernstein